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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,518	05/01/2002	Audrey Goddard	10466/303	8147

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,518	GODDARD ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6, 9-10 and 12-17* is/are rejected.

7)☒ Claim(s) *7,8 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/21/05; 9/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Seq comply*.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05 September 2006 has been entered.

2. Claims 1-5 are cancelled.

Claim 12 has been amended.

3. Claims 6-17 are pending and under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. This office Action contains New Grounds of Rejections.

Information Disclosure Statement

6. The IDS submitted 21 November 2005 and 05 September 2006 have been fully considered. It is noted that Applicant refers to the IDS submitted on 17 November 2005, however, the electronic file only contains an IDS filed 21 November 2005, which the Examiner assumes is the IDS applicant wishes to have considered. Acknowledgement is requested.

It is further noted that the IDS filed 9/10/2002 lists US Patent 5,546,637 to Jacobs, however, US Patent 5,546,637 is issued to Herbert N. entitled "Two-part plastic

clip for closing sausage casings, bags or the like". The relevance of the reference is not clear to the examiner. Applicant should provide clarification and/or provide the correct patent number for consideration by the examiner. Additionally, references 3-4 listed on the IDS filed 9/10/2002 are duplicate citations of references 27-28 filed 5/2/05 and thus, have been crossed out on the IDS field 9/10/2002 to avoid delays at the time of allowance.

Sequence Requirements

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). This application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 because this application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c) a paper copy of the sequence listing.

8. Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the attached Notice to Comply.

9. APPLICANT IS GIVEN THE TIME ALLOTED IN THIS OFFICE ACTION WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In

no case may an applicant extend the period for response beyond the six-month statutory period. Direct the response to the undersigned.

Rejections Withdrawn

10. The rejection of claims 4-17 under 35 U.S.C 101 because the claimed invention is not supported by a substantial asserted utility or a well-established utility is withdrawn in view of the cancellation of claims 4-5 and withdrawn for the following reasons:

The claims of the instant invention are directed to an isolated polypeptide of SEQ ID NO:14. The specification provides several asserted utilities, including that the PRO polypeptides of the present invention may be differentially expressed in a diseased tissue as compared to a normal tissue of the same tissue type.

Applicant states at page 8 of their response that the gene expression data in the specification, Example 18, shows that the mRNA associated with the PRO1864 polypeptide (SEQ ID NO:14) was more highly expressed in melanoma compared to normal skin tissue. Gene expression was analyzed using standard semi-quantitative PCR amplification reactions of cDNA libraries isolated from different human tumor and normal human tissue samples. Identification of the differential expression of the PRO1864 polypeptide-encoding gene in tumor tissue compared to the corresponding normal tissue renders the molecule useful and enabled as a diagnostic tool for the determination of the presence or absence of tumor.

Example 18 at page 140 of the instant specification demonstrates differential expression of PRO1864 cDNA using quantitative PCR amplification reactions.

DNA45409-2511 was shown to be more highly expressed in melanoma compared to normal skin tissue, in this Example. Applicant states at page 12 of the response that Example 18 utilizes a more accurate and reliable method of assessing changes in mRNA levels, namely quantitative PCR analysis (RT-PCR). Applicant relies on more than 140 references (see IDS filed 3/6/2006), where expression levels of mRNA, measured by quantitative PCR, were found to have a good correlation to the expressed protein levels.

It had been previously argued in the previous Office actions that mRNA levels were not predictive of protein levels, citing references by Haynes et al. , Gygi et al., Gokman-Polar., Greenbaum., Lian., Fessler., ect). However, these references were measuring and analyzing mRNA levels using microrarrays, not using quantitative PCR analysis and the art recognizes that the results obtained by microarray are not always the same as the results obtained using quantitative PCR (for example, see Oda et al. Virchows Arch. 430:99-105, 1997, specifically page 104, column 1, paragraph 2). While the PTO found several references in which the protein expression levels did not correlate with mRNA levels measured by quantitative PCR (see Sugg et al., Clinical Endocrinology 49: 629-637, 1998; Toler et al., Am. J. Obstet. Gynecol. 194:e27-e31, 2006; Berner et al. Histopathol. 42: 546-554, 2003 ; Brooks et al. Am. J. Physiol. Renal Physiol. 284: F218-F228, 2003), the majority of the references which were found, including those cited by Applicant, demonstrated a correlation between mRNA levels measured by quantitative PCR and protein expression levels.

Applicant asserts that the expression levels of protein correlate to mRNA (cDNA) levels when the cDNA is measured by quantitative PCR (i.e. RT-PCR). Applicant has provided more than 140 references in support of this position. The prior art of record (Haynes et al., Gygi et al., Gokman-Polar., Greenbaum., Lian., Fessler., ect), argued by the Examiner, is not specifically directed to message levels measured by RT-PCR. Based on the totality of evidence of record, one of skill in the art would find it more likely than not that an increase in message as measured by RT-PCR would be predictive of an increase in protein expression levels, absent evidence to the contrary. Therefore, the data presented in Example 18, which demonstrates differential expression of the nucleic acid encoding PRO1864, also supports a conclusion of differential expression of the PRO1864 polypeptide. Therefore, one of ordinary skill in the art would be able to use the PRO1864 polypeptide diagnostically for distinguishing melanoma from normal skin, as asserted by Applicant.

11. The rejection of claims 4-17 under 35 U.S.C. 112, first paragraph, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention is withdrawn for the reasons set forth above (see item no. 10).

12. The rejection of claims 4-5 and 12-17 under 35 U.S.C 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the cancellation of claims 4-5 and in view of the new grounds of rejection below (see item no. 17 below).

13. The rejection of claims 4-5, 7-8 and 11 under 35 U.S.C. 112, first paragraph, because the specification contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in view of the cancellation of claims 4-5 and upon further consideration.

14. The rejection of claims 4-5 under 35 U.S.C. 112, first paragraph, NEW MATTER, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed is withdrawn in view of the cancellation of the claims.

Response to Arguments

15. The rejection of claims 6, 9-10, 12-17 under 35 U.S.C. 112, first paragraph, because the claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

As an initial matter, Applicant combines their arguments against the above enablement rejection with their arguments against the separate rejection for written description at pp. 29-30 of the response. Applicant is again reminded that the written description requirement is separate and distinct from the enablement requirement. In re Barker, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064

(1978); Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991). See MPEP 2161.

The response filed 9/5/2006 has been carefully considered, but is deemed not to be persuasive. Applicant sates that they have previously addressed Burgess, Lazar, Schwartz, Lin and Li et al and incorporate by reference the previous arguments. The examiner's rebuttal to these remarks is also of record and is incorporated by reference. Applicant also reiterates that there is not substantial variation within the sequences of the claimed polypeptides and applicant maintains that one of skill in the art can readily determine whether a polypeptide can be used to generate antibodies which specifically detect the polypeptide of SEQ ID NO:14 in skin tissue samples. This has been fully considered but is not found persuasive. As discussed above the claim language encompasses a large genus of polypeptides having at least 95% sequence identity to the polypeptide of SEQ ID NO:14 or to fragments of SEQ ID NO:14, i.e., at least 95% sequence identity to an extracellular domain, which embraces polypeptides that differ substantially form the polypeptide of SEQ ID NO:14. For example, a polypeptide that comprises the extracellular domain of amino aids 119-129 of SEQ ID NO:14 would minimally share 10 amino acids with the 234 amino acids of SEQ ID NO:14 and as such would have 4% sequence identity with the polypeptide of SEQ ID NO:14. Applicant is relying upon the disclosure of a single PRO1864 polypeptide (SEQ ID NO:14) and the overexpression of the nucleic acid encoding said polypeptide in melanoma compared to normal skin to support the large genus of polypeptides, which in contrast to applicants arguments embrace widely divergent polypeptide sequences, and which have not been

shown to be more highly expressed in melanomas compared to normal skin. Further, Lederman et al (Molecular Immunology 28:1171-1181, 1991, reference 12 on IDS filed 9/5/06) that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document) and Li et al (Proc. Natl. Acad. Sci. USA 77:3211-3214, 1980,) teach the dissociation of immunoreactivity from other activities when constructing analogs (see entire document). Thus, one of skill in the art could not predictably use the claimed genus of different polypeptides to generate antibodies that specifically detect the polypeptide of SEQ ID NO:14 in skin tissue samples.

Again, at has not provided any guidance to assist the skilled artisan in making and using the claimed polypeptide variants that are 95% or 99% identical to SEQ ID NO:14 or even variants that are 95% or 99% identical to amino acids 21-53, 119-129 or 167-234 of SEQ ID NO:14 or fusion of said portions of SEQ ID NO:14 to the signal peptide of SEQ ID NO:14 (i.e., amino acids 1-20 of SEQ ID NO:14) in a manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions, or substitutions and fragments. Thus, given the substantial variability of the claimed polypeptides relative to the polypeptide of SEQ ID NO:14 and in view of the teachings of Lederman et al and Li et al (as well as Burgess et al, Lazar et al, Schwartz et al and Lin et al, all of record 1/31/05), it would be highly unpredictable that an antibody produced against a polypeptide variant of SEQ ID NO:14 as embraced by the claims would specifically detect the polypeptide of SEQ ID NO:14 in skin tissue samples. Further, complicating the issue is that the polypeptide of SEQ ID NO:14 has not been demonstrated to be more highly expressed in melanomas compared to normal

skin as applicant is relying upon. Further, it is curious that applicant argues the utility of the polypeptide of SEQ ID NO:14 without showing polypeptide expression in melanomas compared to normal skin, yet based upon the same utility, applicant argues the enablement of polypeptide variants of SEQ ID NO:14 that are not encoded by the PRO1864 nucleic acid (DNA454909-2511) actually shown to be "more highly expressed" in melanomas compared to normal skin and it is not known whether such a polypeptide exists. The teachings set forth in the specification provide no more than a plan or invitation for those of skill in the art to experiment practicing the claimed invention; they do not provide sufficient guidance or specificity as to how to execute that plan. At most, the specification will enable those skilled in the art to attempt to discover for themselves how to practice the claimed invention, however, this is insufficient to constitute adequate enablement.

Due to the large quantity of experimentation necessary to generate the polypeptide variants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art (Lederman et al and Li et al, of record), which establishes the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

16. The rejection of claims 6, 10 and 12-17 under 35 U.S.C. 112, first paragraph; as introducing new matter into the claims is maintained.

The response filed 9/5/2006 states that Figure 14 discloses a signal peptide between amino acids 1-20 of SEQ ID NO:14 and transmembrane domains between amino acids 54-72, 100-118, 130-144 and 146-166 of SEQ ID NO:14. The demarcation of these regions of the protein also demarcates the intervening amino acids at positions 21-53, 119-129 and 167-234 of SEQ ID NO:14. This has been fully considered but is not found persuasive. Applicant is correct in that Figure 14 shows the signal peptide and the extracellular domains of the polypeptide of SEQ ID NO:14, however, these portions are in the context of SEQ ID NO:14, whereas the claims embrace polypeptides that comprise the signal domain of SEQ ID NO:14 (i.e., amino acids 1-20) and comprise an extracellular domain selected from 21-53, 119-129 and 167-234 of SEQ ID NO:14 or sequences at least 95% identical thereto. Thus, the claims encompass a genus of polypeptides that comprise the signal peptide of SEQ ID NO:14 fused to an extracellular domain selected from 21-53, 119-129 and 167-234 of SEQ ID NO:14. Applicant still has not pointed to anything in the as filed disclosure that provides adequate written support for polypeptides that comprise amino acids 1-20 of SEQ ID NO:14 and an extracellular domain selected from 21-53, 119-129 and 167-234 of SEQ ID NO:14, that are not the polypeptide of SEQ ID NO:14. The disclosure as filed does not provide clear contemplation of the polypeptides that comprise the signal peptide of SEQ ID NO:14 fused to an extracellular domain selected from 21-53, 119-129 and 167-234 of SEQ ID NO:14. Thus, the disclosure of SEQ ID NO:14 and the identification of the

signal peptide and the extracellular domains of SEQ ID NO:14 as pointed to by applicant does not provide adequate written support for the larger genus of polypeptides comprising amino acids 1-20 of SEQ ID NO:14 and an extracellular domain selected from amino acids 21-53, 119-129 and 167-234 of SEQ ID NO:14, wherein the polypeptides are not SEQ ID NO:14.

The instant claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in claims 6, 10 and 12-17, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claims 6, 10 and 12-17 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

New Grounds of Rejections

17. Claims 6, 9-10 and 12-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction

to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (see MPEP 2163).

The claims are drawn to isolated polypeptides comprising an extracellular domain of the polypeptide of SEQ ID NO:14, wherein the extracellular domain is selected from the group consisting of amino acids 21-53, 119-129 and 167-234 of SEQ ID NO:14 and wherein the polypeptide is fused to a heterologous polypeptide that is a tag polypeptide or an Fc region of an immunoglobulin. Further, the claims are drawn to an isolated polypeptide having at least 95% amino acid identity to the amino acid sequence of SEQ ID NO:2 or an extracellular domain selected from the group consisting of amino acids 21-53, 119-129 and 167-234 of SEQ ID NO:14 and wherein the polypeptide is fused to a heterologous polypeptide that is a tag polypeptide or an Fc region of an immunoglobulin. The transitional terms "comprising" and "having" are open-ended or inclusive to the addition of unrecited elements (see MPEP 2111.03). The specification discloses that the amino acid sequence of SEQ ID NO:14 is 234 amino acids in length and is encoded by a nucleic acid (DNA454909-2511) that is overexpressed in melanoma tumor compared to normal skin (see Fig. 14, and Example 18). However, the scope of the claims includes a genus of isolated polypeptides that comprise the amino acid sequence of an extracellular domain of SEQ ID NO:14 fused to a tag polypeptide or an Fc region of an immunoglobulin, optionally including the signal

peptide (i.e., amino acids 1-20 of SEQ ID NO:14) as well as isolated polypeptides having at least 95% sequence identity to said extracellular domain or at least 95% sequence identity to SEQ ID NO:14, optionally fused to a tag polypeptide or an Fc region of an immunoglobulin and optionally including the signal peptide (i.e., amino acids 1-20 of SEQ ID NO:14). Thus, the claims embrace an extremely large genus of isolated polypeptides having disparate structures/sequences and functions from that of SEQ ID NO:14.

There is insufficient written description for the genus of polypeptides that "comprise" amino acids 21-53, 119-129 and 167-234 of SEQ ID NO:14 or polypeptides that "comprise" sequences that are at least 95% identical to amino acids 21-53, 119-129 and 167-234 of SEQ ID NO:14 or polypeptides that are at least 95% identical to SEQ ID NO:14, wherein the polypeptide is optionally fused to a tag polypeptide of an Fc region of an immunoglobulin because there is no disclosure of the structures/sequences contained therein and one could not predict the operability of the different polypeptides. For example, Lederman et al (Molecular Immunology 28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Li et al (Proc. Natl. Acad. Sci. USA 77:3211-3214, 1980) disclose that dissociation of immunoreactivity from other activities when constructing analogs (see entire document). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." *In re Curtis*,

354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). Thus, the ordinary skilled artisan could not predict whether an antibody raised against an isolated polypeptide or fragment thereof "comprising" amino acids 21-53, 119-129 or 167-234 of SEQ ID NO:14, or an isolated polypeptide "having" at least 95% sequence identity with SEQ ID NO:14 or 95% sequence identity with amino acids 21-53, 119-129 or 167-234 of SEQ ID NO:14 could be used to specifically detect the polypeptide of SEQ ID NO:14 in melanoma and skin tissue samples. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., *Eli Lilly*.

Further, it is not sufficient to define it solely by its principal biological property, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Per the *Enzo* court's example, (*Enzo Biochem, Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (CA FC 2002) at 1616) of a description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) couched "in terms of its function of lessening inflammation of tissues" which, the court stated, "fails to distinguish any steroid from others having the same activity or function" and the expression "an antibiotic penicillin" fails to distinguish a particular penicillin molecule from others possessing the same activity and which therefore, fails to satisfy the written description requirement. Similarly, the asserted function of being used to generate antibodies, which can be used to specifically detect the polypeptide of SEQ ID NO:14 in skin tissue, fails to distinguish any polypeptide from others having the same function and as such, fails to satisfy the written-description requirement. Mere

idea or function is insufficient for written description; isolation and characterization at a minimum are required. A description of what a material does, rather than what it is, usually does not suffice. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Structural features that could distinguish a polypeptide in the genus from others in the protein class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Since the disclosure does not describe the common attributes or structural characteristics that identify members of the genus, and because the genus is highly variant, the function of being used to produce an antibody to specifically detect SEQ ID NO:14 in melanoma and skin tissue alone is insufficient to describe the genus of polypeptides that function equivalently. One of skill in the art would reasonably conclude that the disclosure of a single polypeptide, i.e., SEQ ID NO:14, does not provide a representative number of species of isolated polypeptides that minimally comprise an extracellular domain (i.e., amino acids 21-53, 119-129 or 167-234) of SEQ ID NO:14 or polypeptides that are at least 95% identical to SEQ ID NO:2 or an extracellular domain thereof to describe the claimed genus of polypeptides and antibodies that bind such. The recitation of amino acids 119-129 of SEQ ID NO:2, comprising only 11 of the possible 234 amino acids of SEQ ID NO:14 for example, does not convey a common structure nor a common function because there is no description of the sequence/structure of the remaining 223 amino acids or more. As such, generic polypeptide sequences that are unrelated via structure and function are highly variant

and not conveyed by way of written description by the specification at the time of filing. As such the specification lacks written description for the highly variant genus of single function polypeptides (antibody binding) and one skilled in the art would not recognize that applicants had possession of the genus of claimed polypeptides for antibody binding as instantly claimed.

Therefore, only the isolated polypeptide set forth in SEQ ID NO:14, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Response to Arguments

The response filed 9/5/2006 has been carefully considered, but is deemed not to be persuasive. Applicant maintains that the instant claims are analogous to the claims discussed in Example 14 of the written description training materials, in which written description was found to be satisfied for claims relating to polypeptides having 95% homology to a particular sequence and possessing a particular activity, even though applicant had not made any variants. This has been fully considered but is not found persuasive for reasons already of record. Again, unlike example 14, which encompasses a genus of molecules having significant structural similarity and a defined biological function, the genus of polypeptides of the present claims may have functions and structures that differ greatly from that of PRO1864 as there is no disclosed functional or biological activity. Therefore, one of skill in the art would not be able to

identify the encompassed molecules as being identical to those instantly claimed. Further, the specification does not describe the structural features of any polypeptides that only comprise an extracellular domain of SEQ ID NO:14 or polypeptides that are 95% or 99% identical to SEQ ID NO:14, that are more highly expressed in melanomas compared to normal skin. Also, unlike Example 14 of the written description training materials, the polypeptide of SEQ ID NO:14 is not disclosed as having any particular function or biological activity. Conception does not occur unless one has a mental picture of the structure of the molecule, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it.

Additionally, unlike Example 14 of the written description training materials the instant claims encompass polypeptides where the only distinguishing characteristic is partial structural identity with SEQ ID NO:14, such as a polypeptide comprising an extracellular domain selected from amino acids 21-53, 119-129 and 167-234 of SEQ ID NO:14. Thus, the claims are drawn to polypeptides having at least 95% amino acid identity with only 11 amino acids (i.e., 119-129) out of the 234 amino acids of SEQ ID NO:14. Clearly, and contrary to applicants assertion there is substantial variation within the species which fall within the genus. There is no functional limitation with respect to these partial structures of SEQ ID NO:14 and as above, the encompassed polypeptides may have substantially different structures and biological functions. This is not similar to example 14 of the written description training materials, which is drawn to polypeptides having 95% homology to a particular sequence and possessing a

particular catalytic activity, which uniquely distinguishes members of the genus by structure and function. The only distinguishing characteristic of the present claims is sequence identity or partial sequence identity in the case of the "extracellular domain", optionally comprising the signal peptide of SEQ ID NO:14.

Conclusions

18. Claims 7-8 and 11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

Application No. 10/063,518

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other: _____

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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